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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,130	09/21/2000	John W. Barnwell	5986/17686-US5	8596

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Darby & Darby P C  
805 Third Avenue  
New York, NY 10022

EXAMINER

DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 03/26/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/667,130

Applicant(s)

Barnwell

Examiner

Patricia A. Duffy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jan 2, 2003
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 22 and 23 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22 and 23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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***Response to Amendment***

1. The response filed 1-2-03 has been entered into the record. Claims 22 and 23 are pending and under examination. Please note the new grounds of rejection set forth herein.
2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

***Information Disclosure Statement***

3. The information disclosure statement filed 1-2-03 is confusing to the prosecution record of this application. Applicants provided an initialed copy of list of references in a previous parent application. The installed 1449 is from another application, it has been place in the file. The list of references thereon have been considered, but a initialed 1449 will not be provided until applicants provide a proper 1449 directed to this specific application that is a listing of references that have not been previously initialed, signed and dated. The presence of an initialed 1449 renders the prosecution history of this file confusing because it was not pending in 1996. As such, should Applicants wish the listed references to be printed on the face of any patent that issues from this application, they should provide a clean copy of a 1449 that is directed to this application but is not already signed and dated.

***Rejections Withdrawn***

4. The substitute specification has been entered into the record. The claimed priority is now reflected in the first line of the substitute specification.
5. The objection to the title is withdrawn based on Applicants amendment.

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6. The formal drawings were received on 1-2-03. These drawings are approved by the draftsman.

*Objections/Rejections Maintained*

7. The preliminary amendment filed 9-21-00 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "EcoRI digest of purified ..... for 2 months." which is inserted at page 5, line 18 after "1989". The objection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

Applicants arguments and the declaration have been previously extensively considered but were not persuasive and remain not persuasive. Declarant attests that any set of conditions set forth in Southern et al would have resulted in selection of a hybrid between a nucleic acid of interest to an investigator and is complement. This is not persuasive, Southern et al does not discuss stringency. Declarant's opinion is not supported by the discussion of Southern et al. Southern et al is a discussion of a variety of factors including time, temperature, salt concentrations that effect hybridization/annealing of one nucleic acid to another. As quoted by Applicants any hybridization condition of Souther et al would be considered "stringent" because it would have resulted in selection of a hybrid. This is not persuasive it presents an unsubstantiated conclusion "... any set of disclosed conditions would have resulted in selection of a hybrid between a nucleic acid of interest to an investigator and its complement". Further, it appears to argue that any hybridization conditions are considered "stringent". As subsequently argued by Declarant the concept of stringency

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(i.e. the concept that the intrinsic specificity of the hybridization reaction depends on the annealing conditions employed) is not set forth in Southern et al and not discussed therein. Applicants declaration of concepts allegedly known in the art, but not documented and moreover not specifically set forth and discussed by Southern et al are not persuasive. Applicants argue that the MPEP 608.01(p) is merely a guideline and not an absolute and the case law supports Applicant's position and is reiterated by Applicants. This again was not persuasive for the following reasons made of record. "The present case is different from the "Hawkins" decisions, different from *In re Voss*, 194 USPQ 144 (CCPA 1973) and *In re Fouche*, 169 USPQ 429 (CCPA 1971). In *In re Voss*, the court cited *In re de Seversky* 474 F.2d 671, 177 USPQ 144 (CCPA 1973), where the requirements for an incorporating references were clearly set forth. The incorporating statement must clearly identify the subject matter to be incorporated and where it is to be found. In the instant case these requirements are not met by the specification passage of page 5, lines 15-20. Since the entirety of the reference is cited, it is also unclear which portion(s) of the reference applicant rely upon or specifically where in the reference they are to be found. The subject matter to be incorporated cannot clearly be identified by a mere reference to the entirety of a citation." In contrast to Applicants assertion, the statement in the specification is not reasonably precise, it cites a concept and an alleged definition of conditions that are not discussed or defined in Southern et al. There is no precision in the incorporation by reference statement recited in the specification. Applicants argue that a true copy of the Hawkins declaration was filed with this continuing application and provide an additional copy as Appendix 4. The examiner thanks Applicants for the additional copy of the Hawkins declaration to complete the prosecution record in this application. Applicants assert that the Examiner has also misinterpreted the Crother's Declaration and

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that stringent conditions are a combination of temperature and salt conditions. This is not persuasive. The declaration of Dr. Crother's clearly indicates that "stringent conditions" are a definition of conditions based on the melting temperature of the hybrid duplex. "Stringent hybridization is typically carried out at the temperature that maximizes the hybridization rate..." and "Generally this temperature occurs about 20 degrees Celsius below the melting temperature of the hybrid duplex...". As such, the alleged stringent conditions depend on the specific melting temperature of the hybrid duplex. Therefore, alleged stringent conditions depends on the melting temperature of the nucleic acid forming a hybrid with SEQ ID NO:1. As such, there is no "typical" hybridization conditions, the conditions are defined in relation to a particular SEQ ID NO and the characteristics of the hybrid desired and as such are necessarily empirical in nature and are defined by the hybrid itself. The combination of salt and temperature conditions are defined in essence by the hybrid and its melting temperature. The melting temperature of any hybrid is empirical in nature and not set forth in the specification. The salt and temperature conditions of Southern et al were *empirically set for the nucleotides used therein*. Since the instantly claimed SEQ ID NO:1 is not identical to the nucleic acids used in Southern et al and the hybridization of any nucleic acid would depend on the melting temperature of the hybrid, the conclusion that the rates of hybridization would be identical is not supported by the literature. Stringency is defined by the "hybrid under study" and is empirical in nature and is defined by the structure of hybridizing nucleic acid. One selects hybridization conditions to determine the extent to which the reaction conditions allow only completely complementary structures to form. As such, the nature and structure of the hybrid does in fact determine what is considered "stringent" conditions or not. "Stringent conditions" as argued by Applicants do not provide for

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specificity of hybridization because it depends on the calculated  $T_m$  of the hybrid under study and can be determined empirically and hybridization allows for mismatches.

Stringency is a term and concept of degree and is not set forth nor discussed in Southern et al. Applicants essentially argue that any combination of salt and temperature provides for stringent conditions. However, stringency refers to the extent to which the reaction conditions allow only completely complementary structures to form and thus is defined by the structure of hybrid. Delecarant's opinion as to the conditions in Southern defined as stringent lacks evidentiary support. As previously set forth "the passage clearly indicates that ""Stringent conditions" are as defined by [emphasis added] Southern et al....". The operative word here is "by". Southern et al defines no "stringent conditions", nor does Southern et al refer to any particular set of conditions which are "stringent". Southern et al describes multiple examples of hybridization conditions (see for example page 507, lines 7-11, page 510, figure legend, page 510, Table 2, page 511, Figure 5, variation in temperatures of hybridization, page 511, Figure 6, variation in time of hybridization, page 515, figure legend). The passage of the specification fails to provide direct one skilled in the art to the specific hybridization conditions now inserted into the specification and claims.

The rejection is maintained.

8. Claims 22 and 23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 26 and 28 of copending Application No. 08/719,821. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of full complements claimed in the copending application, would by definition hybridize to SEQ ID NO:1 and thus anticipate the instant genus claims. The rejection is maintained for reasons made of

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record in Paper No. 8, mailed 7-1-02. Applicants indicate that a terminal disclaimer would be filed upon indication of allowable subject matter. The provisional rejection is maintained until resolution by terminal disclaimer.

9. Claim 23 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

Applicants argue that this is the same issue addressed in regard to the objection to the specification and is therefore should be withdrawn. This is not persuasive for reasons made of record previously and Applicant's arguments with respect to the insertion of new matter into the specification were not persuasive for reasons set forth above.

10. Claim 22 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

Applicants argue that this is the same issue addressed in regard to the objection to the specification and is therefore should be withdrawn. This is not persuasive for reasons made of record previously and Applicant's arguments with respect to the insertion of new matter into the specification were not persuasive for reasons set forth above.

11. Claims 22 and 23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sigma Molecular biology Product Guide, 1991, pages 54-56). The rejection is maintained for reasons made of record in Paper No. 8, mailed 7-1-02.

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Sigma et al teach isolated and purified oligo-d(pA) and oligo-d(pT) oligonucleotides. Each of the oligonucleotide products share 100% identity with at least residues 193-221 of SEQ ID NO:1. Applicants arguments have been carefully considered but are not persuasive. The prior art compounds have a region of 22 consecutive identical nucleotides in common with SEQ ID NO:1 as previously cited. It is well established in the art that it merely takes a region of 10 consecutive nucleotides in length to provide for stable hybrid formation. It is also well established in the art that the thermal stability rises sharply for longer lengths and the stability of a complementary duplex of 25-50 nucleotides approaches that of any much longer complex. As such, the prior art oligonucleotides would hybridize absent convincing factual evidence to the contrary. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the nucleic acids of the prior art does not possess the same functional characteristics of the claimed nucleic acid). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

***New Rejections Based Written Description Guidelines***

12. Claims 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

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The specification discloses that the nucleic acid of SEQ ID NO:1 is a DNA identified using an expression cloning of the Plasmodium vivax antigen that binds the mAb1D11.G10 antibody. The DNA encodes an antigen that is diagnostic for the presence of the pathogen Plasmodium vivax (see page 4 and page 9, second full paragraph and pages 25-26 Example 6).

The claims are drawn to isolated and purified nucleic acids that hybridize under stringent conditions or under specific conditions. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

After further review, it is noted that SEQ ID NO:1 is a genomic DNA fragment. Further, the specification does not disclose that SEQ ID NO:1 is drawn to a full length open reading frame and specifically teach that it is a fragment. The specification states that "The gene appears to be missing a small portion of the 5' end." and moreover suggests that "Completion of the 5' gene sequence will shed more light on these possibilities,...". teaches that (page 8, lines 7-22). The claims reciting the "comprising" read upon complete gene sequences having in common a nucleotide sequence of SEQ ID NO:1 from any source. With the exception of a nucleic acid consisting of SEQ ID NO:1, the skilled artisan cannot

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envision the detailed chemical structure of the encompassed polynucleotides, regardless of the simplicity of the method of isolation, absent further guidance. Since the claimed genus encompasses undisclosed genes, partial genomic sequences, and genes yet to be discovered, the disclosed structural feature (i.e., the nucleic acid consisting of SEQ ID NO:1) does not constitute a substantial portion of the claimed genus. Absent a written description disclosing a representative number of nucleic acid sequences from this broad class of polynucleotides, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed.

In addition, the claims comprising a sequence which hybridizes under stringent conditions or specific stringent conditions to a nucleic acid comprising a sequence as set forth in SEQ ID NO:1 as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature of the instantly recited nucleic acids, nor a correlation between a particular structure and function. The genus of nucleic acid probes which would hybridize to a nucleic acid comprising SEQ ID NO:1 is very large, encompassing not only sequences with polymorphisms and mutations compared to SEQ ID NO:1, but also sequences having no shared sequence with SEQ ID NO:1 itself since the hybridization could occur within the non-SEQ ID NO:1 portion of the nucleic acid comprising SEQ ID NO:1. Further, no function is required of this hybridizing nucleic acid. Thus the genus of nucleic acids encompassed by this claim is extensive, and there does not appear to be any requirement that the nucleic acid to share either a particular structure, a particular function, nor a correlation between some partial structure and a particular function. Consequently, SEQ ID NO:1 again does not appear to constitute a substantial portion of the claimed genus. Since these various hybridizing nucleic acids do not possess defined structures, fragments

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of these nucleic acids also lack adequate written description, as do vectors, host cells and kits comprising.

The genus of nucleic acids encompassed by the instant claims is much more extensive than SEQ ID NO:1 itself or internal fragments of SEQ ID NO:1 that could be used as probes or primers. The instant claim language opens up the claims to "flanking" sequences of undisclosed structure/sequence and unlimited length. It is because of this open language that the specification fails to provide an adequate written description of the instant claims. The mere statement that a genus of nucleic acids is part of the invention and reference to a potential method for isolating some of these nucleic acids is not adequate written description of those nucleic acids. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Consequently, Applicant was not in possession of the instant claimed invention. Further, Reagents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398, appears to be directly relevant to the instant fact pattern. In Eli Lilly the specification and generic claims to all cDNAs encoding for vertebrate or mammalian insulin did not describe the claimed genus because they did not set forth any common features possessed by members of the genus that distinguished

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them from others. Id. at 1568, 43 USPQ2d at 1405. Nor did the specification describe a sufficient number of species within the very broad genus to indicate that the inventors had made a generic invention, i.e., that they had possession of the breadth of the genus, as opposed to merely one or two such species. Id. In the instant case, Applicant has described a single species (the nucleic acid consisting of SEQ ID NO:1), but is attempting to claim an extremely broad genus of nucleic acids which do not necessarily share any common feature with SEQ ID NO:1.

#### *Status of Claims*

13. All claims stand rejected.

#### *Conclusion*

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

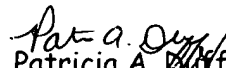
Patricia A. Duffy, Ph.D.

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March 21, 2003

  
Patricia A. Duffy, Ph.D.  
Primary Examiner  
Group 1600